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Michael O. Leavitt, Administrator
US Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Comments on the HPV test plan for Alcohols, C4, distn. Residues

Dear Administrator Leavitt:

The following comments on the BASF test plan for alcohols, C4, distn. residues are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

Toxicology and Regulatory Affairs, on behalf of BASF, submitted its test plan on December 31, 2003 and June 8, 2004 for the chemical mixture alcohols, C4, distn. residues, also known as "butanol bottoms" or EP-202MP (CAS RN 68551-11-1). We will refer to the mixture in these comments as EP-202MP. According to the test plan, this mixture is made up of several known and unknown aliphatic hydrocarbons; the primary components are 2-ethylhexenal and 2-ethylhexanal, which make up approximately 20% of the mixture. From page 7: "The High Production Volume (HPV) mixture produced by BASF and described in this document is restricted to the high-boiling fraction derived from the hydroformylation of propene." The mixture is manufactured in a site-limited, closed system fashion, and is used as a chemical solvent and a heat generator. Human exposure is limited to occupational sampling and loading/unloading of the chemical from railcars and tank-trucks. However, workers use personal protective equipment during handling. Especially given the mixture components' low volatility and odoriferous warning properties, the potential for human injury as a result of significant exposure is very low.

Although it seems odd that some of EP-202MP's components are unknown, the opportunity for hazard characterization is still good. This is because the process of manufacture that dictates the remaining residues from distillations that comprise the mixture is well characterized. In the production of aldehydes and alcohols, the higher molecular weight compounds that are the distillation residues of these processes are combined to form the final mixture. To further confirm the relative homogeneity of the mixture, a ^{13}C-NMR spectrum was recorded, and shows a lack of aromatic carbon species.

BASF has fulfilled all requested test endpoints using existing data from several known components of the mixture. The component most commonly relied upon is 2-ethylhexanol (104-76-7), but data from 2-ethyl-1,3-hexanediol (94-96-2), 2-ethylhexanal (123-05-7), EP-202MP itself, butyraldehyde (123-72-8), n-butanol (71-36-3), and 2-etheylhexenal (645-62-5) are also used in the test plan.

Multiple components of the mixture are used to fulfill all HPV requirements for ecotoxicity. Structure-activity relationships and known metabolic relationships and pathways reveal that the component 2-ethylhexanol best predicts systemic health effects of the mixture. Since data are available for 2-ethylhexanol and several other components of the mixture (listed above), no further testing is proposed for human health effects endpoints. Data is available for multiple methods of administration (feeding, gavage, inhalation, and dermal), and multiple species (rat, rabbit, and guinea pig), sometimes for a single endpoint. Since aldehydes might exhibit contact toxicity in addition to or not predicted by 2-ethylhexanol, BASF has also included dermal toxicity information for butyraldehyde, another mixture component. Although a formal reproductive study is not available for 2-ethylhexanol, BASF uses a weight-of-evidence approach, combining histopathology of reproductive organs from sub-chronic and chronic studies with a negative developmental study. A reproductive study was conducted on DEHA, which is a progenitor to 2-ethylhexanol, and was shown to be generally non-toxic to reproductive endpoints. 2-ethylhexanol, DEHA, and di-2-ethylhexyladipate, another surrogate for 2-ethylhexanol, have been investigated dermally and orally for developmental toxicity.

This test plan is an example of the type of thorough literature research and thoughtful toxicology that is needed to be consistent with the EPA's stated goal of maximizing the use of existing data in order to limit additional animal testing and to avoid a mere box-checking approach to the HPV program. Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 335, or via e-mail at kstoick@pcrm.org.

Sincerely,

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Research Analyst

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